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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/688,254	10/13/2000	Harry M. Meade	10275-139001	9900
26161	7590	01/29/2004	EXAMINER	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			QIAN, CELINE X	
			ART UNIT	PAPER NUMBER

1636

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/688,254

Applicant(s)

MEADE ET AL.

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5,6,8-10,12-14 and 19-36 is/are pending in the application.
- 4a) Of the above claim(s) 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5,6,8-10,12-14 and 20-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 November 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- ☐ Interview Summary (PTO-413) Paper No(s). _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other:

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DETAILED ACTION

Claims 5, 6, 8-10, 12-14 and 19-36 are pending in the application. Claim 19 is withdrawn from consideration for being directed to non-elected subject matter. Claims 5, 6, 8-10, 12-14 and 20-36 are currently under examination.

This Office Action is in response to the Amendment filed on 11/10/2003.

Response to Amendment

The rejection of claim 25 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment of the claim.

The rejection of claims 20 and 26 under 35 U.S.C. 112 1st paragraph (new matter) is maintained for reasons set forth of the record mailed on 2/7/03 and further discussed below.

The rejection of claims 9, 10, 21, 22 and 28 under 35 U.S.C. 112 1st paragraph (written description) is maintained for reasons set forth of the record mailed on 2/7/03 and further discussed below.

The rejection of claims 5, 6, 8-10, 12-14, 21-25 and 27-30 under 35 U.S.C. 103 (a) is maintained for reasons set forth of the record mailed on 2/7/03 and further discussed below.

Newly added claims 31-36 are rejected under 35 U.S.C. 112 1st paragraph (new matter) for reasons discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 9, 10, 20-22, 26 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant requests a basis for this rejection.

The reasons for this rejection are discussed in detail on page 3 and 4 of the previous office action mailed on 2/7/03. Claims 20 and 26 are rejected for new matter, and claims 9, 10, 21, 22 and 28 are rejected for written description.

In response to the new matter rejection of claims 20 and 26, Applicant argues that “the third binding moiety” is supported by the claims and specification as originally filed. Applicant argues that the term “multivalent” is used throughout the specification, and the use of the terms “multivalent” in reference to “binding moieties” should be given their meaning in the field for the production of polypeptides of interest that contain within them multiple binding sites. Finally, Applicant argues that the specification implicit described a genus, “multivalent,” leads to the claiming of a species, “the third binding moiety.”

These arguments have been fully considered but deemed unpersuasive. Although the term “multivalent” is used throughout the specification, the specification fails to describe a transgenically produced multivalent polypeptide comprises a first binding moiety that binds the bindable epitope of the target polypeptide, a second binding moiety that binds a matrix, and a third binding moiety that is capable of removing the bindable epitope from the target polypeptide. The term “multivalent” may imply that the polypeptide can bind different moiety,

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but such description is not sufficient to support the claimed subject matter. Therefore, the claims contain new matter, and the rejection is maintained.

In response to the written description rejection as applied to claims 9, 10, 21, 22 and 28, Applicant argues that the “functional fragment thereof” in reference to specific proteins is supported by the instant specification. Applicant argues that the functional aspects of these fragment is limited for their ability to be used as tools for purification. Applicant further cites three reference to illustrate the functional aspects of fusion proteins changed to aid in the purification efforts is known in prior art. Lastly, Applicant argues that the level of skill in the art is high, and the uses disclosed in the specification is only needed to be communicated to the skilled artisan of the relevant technology, need not be apparent to everyone for the enablement of the claims.

The above arguments have been fully considered, but they are not persuasive. As discussed in the previous office action, in analyzing whether the written description requirement is met, it is determined whether a representative number of species have been described by their complete structure or other relevant identifying characteristics. Applicant is reminded that even the functional aspects of the claimed “chemically functional fragment thereof” are known, the structural aspects of such fragments are not described by the instant specification. As such, the structural functional relationship is missing. The cited references describes the factor X and CBD for its use as fusion protein in protein purification. The claimed genus encompasses “chemically functional fragment” of protein L, any kind of antibody and CBD, which is a large genus compare to what is described in those references. Thus, the specification fails to describe

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a representative number of species by their complete structure nor other identifying characteristics. Therefore, the written description requirement has not been met.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 5, 6, 8-10, 12-14, 21-25, 27-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (5,981,714), in view of Scharwz et al. (5,719,269), Radford et al. (5,955,270), Wagner et al. (6,329,209), Vola et al., (1994, Cell Biophysics 24/25, p.27-36 abstract), Meade et al. (5,750,172), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807).

In response to this rejection, Applicant argues that Cheng et al. fails to teach a) milk or similar bodily derived substance; b) purification of a transgenically derived molecule using a second transgenically derived molecule; or c) modifying a polypeptide sequence to make purification easier through the use of known binding domains. Applicant further argues that Schwartz et al. also fails to teach the above information, and in addition, Schwartz fails to teach milk as a reaction mixture. Moreover, Applicant argues that neither of Radford, Wagner, Vola, Meade and Nuijens reference remedies these deficiencies. Applicant asserts that the field covered by these references is broad and disparate. Applicant also asserts that the large number of references used in this rejection also bears testimony that the invention is not obvious.

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Further, Applicant argues that there is no motivation taught by the cited references to combine the teaching, and the rejection is based on hindsight reasoning. Applicant thus concludes that the claimed invention is not obvious in view of the prior art.

These arguments have been fully considered but deemed unpersuasive. The detailed teaching of the cited references was discussed in detail in the previous office action (page 5-7). The reasons for obviousness of the claimed invention in view of the prior art were also discussed in detail in the previous office action (page 7-9). Contrary to Applicant's assertion, point a) is taught by Nuijens et al. and Meade et al., who teach that the production of recombinant proteins in transgenic animal milk; and point c) is taught by Schwartz et al. and Radford et al., who teach modifying a polypeptide sequence by adding binding domains for purification purpose. Although point b) is not taught by any reference alone, the combined teaching of Cheng et al., Schwartz et al. and Nuijens et al. render this invention obvious for reasons discussed in detail in the previous office action (see page 7, 3rd paragraph, for example).

In response to Applicant's argument that the cited art is broad and disparate, the Examiner respectfully disagrees. The cited references are all in the field of molecular biology and protein purification. They are directly related to the claimed invention, that is, purifying recombinant protein from the milk or other bodily fluid of a transgenic animal. MPEP 2145 states "a prior art reference is analogous if the reference is in the field of Applicant's endeavor or, if not, the reference is reasonably pertinent to the problem with which the inventor was concerned. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992)." In this case, all the references are directly related because they are all directed to protein purification and

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producing recombinant protein in transgenic animal (which would require subsequent protein purification. Such combination of references is analogous to the claimed invention.

In response to Applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

In response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Meade et al. teach the production of recombinant proteins in mammalian milk is feasible and the protein is structurally same as the natural occurring polypeptide. Such teaching provides the basis for combine the teaching of transgenically production of recombinant protein in milk and purification the protein product from the milk. Therefore, the prior art does suggest a clear motivation to combine the references and make the claimed invention.

In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the

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applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As discussed in the previous office action and above, there is a clear motivation to combine the references, and the teaching of the references provides reasonable expectation of success to make the claimed invention. Therefore, the claimed invention is *prima facie* obvious in view of the cited prior art, and the rejection is maintained.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 112

Claims 31-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly added claims 31-36 contain new matter. The instant specification does not disclose that the multivalent polypeptide is used in an ELISA format, the reaction mixture is semi-solid, and the target polypeptide is purified to more than 90% purity. Therefore, the claims are rejected for constitute new matter.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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This application contains claim 19 drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER